Reichert (E. J.)

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ANÆSTHETIC AGENT;

WITH A CONSIDERATION OF ETHYLENE METHYLETHYLATE, ETHYLENE ETHYLATE, ETHYL NITRATE, AND ETHYLIDENE BICHLORIDE.

By EDWARD T. REICHERT, M.D.

[*REPRINTED FROM THE PHILADELPHIA MEDICAL TIMES FOR MAY 7, MAY 21, AND JUNE 4, 1881.*]

ETHYLENE BICHLORIDE AS AN ANÆSTHETIC AGENT;

WITH A CONSIDERATION OF ETHYLENE METHYLETHYLATE, ETHYLENE ETHYLATE, ETHYL NITRATE, AND ETHYLIDENE BICHLORIDE.

ETHYLENE BICHLORIDE, or ethene bichloride, or better known as "Dutch Liquid," and isomeric with the ethylidene bichloride, or ethidene dichloride, which has lately attracted attention through the investigations of the British Medical Association Committee, was first used by Simpson as an anæsthetic agent, and more recently by Nunnelly,* who, after making fourteen experiments on the lower animals and a number on his own students and patients, states that he found it in every way agreeable. In mammals thirty or forty minims were sufficient to cause complete anæsthesia in from two to five minutes, and with a like quantity six out of seven students were rendered completely insensible, although a second dose of twenty minims was occasionally given. In six surgical cases he used it with perfect success, and later in his paper concludes that chloroform is in no respect superior, for the animals were rendered perfectly anæsthetized in quite as short a time, showed no uneasiness while passing into this condition, remained perfectly still while in it, and, in recovering, were altogether free from any unpleasant symptoms; and, further, that if animals were rendered so profoundly anæsthetized by chloroform as with it, they would not have recovered, and that although just as small a quantity would cause anæsthesia as would chloroform, yet a much larger quantity was required to destroy life, and hence its greater safety. Simpson,† who had previously used it, stated that when its vapor was inhaled it caused so much irritation in the throat that but few persons could endure inhaling it until anæsthesia was produced. He, however, certifies that he has seen it inhaled perseveringly until anæsthesia and its usual phenomena were present, and that this condition was not attended with any excitement of the pulse or subsequent headache, and when he took it himself it produced such a degree of irritation in the throat that it did not disappear for many hours. Snow‡ found it to be a powerful agent, but deems it unsafe.

Although not much in the way of recommendation can be said for this preparation from the results of Simpson's and Snow's investigations, yet if we are to judge from those of Nunnelly it must be certain that in so far as its anæsthetic properties are concerned nothing more could be desired; and, indeed, the only objections urged by the two former investigators are its irritancy and its dangerousness. That Simpson laid entirely too much stress on the first of these objections must be inferred, because Nunnelly found it very pleasant to inhale; and so far as my personal acquaintance with the drug is concerned, both in regard to its administration to others as well as personally, it is certain that, while it does possess irritant properties, and does cause distress when first inhaled, the distress is certainly nothing like as severe as we are led to infer, nor is it much, if any, worse than that caused by the inhalation of ether; and as regards the dangerousness of the ethylene, a difference in opinion as to the degree of its dangerousness is also apparent. Still, it will be admitted that the weight of the evidence in its favor or disfavor rests with the assertion of Nunnelly, who made the most elaborate and detailed study, and, with such a decided recommendation, it is apparent that its reintroduction to the profession is but a matter of time. It therefore seems that the present is a fitting occasion for the reconsideration of this compound, and for a detailed study of its

* Transactions of the Provincial Medical and Surgical Association, xvi., 1849, p. 208.

† Edinburgh Medical Journal, viii., 1848, p. 740.

‡ Anæsthetics.

properties as an anæsthetic agent, because we find the confidence in chloroform so universally shaken, the slowness, uncertainty, and many other practical disadvantages of ether so keenly felt, and that the anæsthetics recently introduced, and which were oftentimes lauded to the highest tension, have miserably failed to fulfil the promises made for them, and have even added their victims to the already ghastly anæsthetic holocaust. Hence the profession is eagerly searching for a compound which will prove to be as safe as ether and to possess all the advantages of chloroform; and, while such a stimulus exists for research and experimentation with this class of compounds, we must expect, even at this time, when the physiological laboratories of our institutions of medical learning are open for original research, and scarcely any investigator can plead an absence of facilities for vivisection, to find those who are so utterly reckless as to imperil the lives of their patients by experimenting on them before a proper physiological study has been made on the lower animals and the anæsthetic satisfactorily proven to be safe. How it is that these workers of death presume to be invested with the moral and legal right to unnecessarily jeopardize the lives of their patients is inexplicable.

From this it will be understood that the object of the writer in the preparation of this paper was to determine by an experimental investigation on the lower animals as to whether or not this anæsthetic especially, which appears so promising, is a safe one to use on the human being, and if it does possess any decidedly dangerous properties to point them out, so that if necessity or preference should ever call for its use we will be forearmed by being forewarned, and thus, anticipating certain dangerous results, can meet them promptly and efficiently. And, when it is considered that the degree of dangerousness of any anæsthetic lies practically in its effects on the circulation, the amount of labor necessary to satisfactorily determine this point is not so formidable as it would at first appear. All anæsthetics certainly do depress the sensory nerves or centres, and especially so, the cerebral centres. It is therefore obvious that we cannot hope for a preparation of this class which will not have a tendency to cause death by overwhelming certain vital portions of the nervous system and thus secondarily causing asphyxia or shock; yet the warning of asphyxia is generally so apparent that a fatal result can be avoided. But, on the other hand, where we have a compound which exerts an independent depressant action on the heart besides, we have a double danger to deal with; and that the large majority of deaths following the use of chloroform and bichloride of methylene were due either to a paralysis of the heart alone or to secondary results because of such a depression, by which the already depressed nervous centres are further depressed or paralyzed on account of an inefficient supply of blood, must be apparent; and, while it is practically out of the question to even hope for an anæsthetic which will not cause death by paralyzing the nervous centres and thus causing shock or asphyxia, our one hope still lies in the effort of avoiding those preparations which decidedly depress the heart and which past experience has taught to be invariably dangerous, and of obtaining a compound devoid of this dangerous quality.

In the present investigation three modes of giving the ethylene bichloride were employed: 1st, by inhalation by means of a Woulfe bottle, by which method the air which the animal inhaled was compelled to pass through the bottle having in the bottom either the ethylene alone or numerous pieces of sponge saturated with it, the tube for the entrance of the air running almost to the bottom of the bottle, and the exit-tube being very short and merely extending to the bottom of the cork, so that the air which the animal breathed was always more or less saturated with the ether; 2d, by inhalation from a muslin cone held closely over the tracheal tube or nostrils; 3d, by intravenous injection.

General Action.—In normal animals, and when administered by the use of the usual muslin or linen cone, there are, as with most anæsthetics, three distinct stages,—excitant, anæsthesia, and profound narcosis. With the ethylene we have struggles, general symptoms of intoxication, and blunted sensibility, a quickened pulse and accelerated respirations. Consciousness, sensibility, voluntary motion, and reflex action become rapidly annulled; and the animal lies perfectly relaxed, and is thoroughly anæsthetized. If the inhalation is persisted in, profound narcosis rapidly supervenes, the pulse and

respirations fail, and death ensues from a failure of the latter. The pupils may at first be dilated, but are afterwards contracted, and the further the anæsthetization is pushed the more fully they become so, unless it be in the last of the profound narcosis stages, when, preceding death, they have been observed occasionally to become dilated. Sensibility is invariably lost before motion, and I have almost unexceptionally seen muscular movements occur—not infrequently like clonic convulsions—after the complete abolition of orbital reflexes. It also appeared that the cerebral functions were more seriously affected before other parts of the system.

Early in my experiments I learned that in order to know whether an animal was completely anæsthetized it was not necessary to consult the conjunctiva, *but merely to watch the respirations, for just so soon as they became very frequent the animal was either anæsthetized or so near and rapidly approaching that condition that the inhaler could be removed and the operation proceeded with.* If after the second stage is very pronounced the administration of the ethylene be continued, *the animal invariably dies from a failure of the respiration, and never in a single instance could I induce death by a stoppage of the heart by the inhalation of the vapor, no matter how concentrated the vapor was.*

The dose required to produce anæsthesia was about the same as chloroform, for the difference was so slight as to be unnoticeable.

The Pulse.—The pulse-rate is invariably and decidedly increased, even in the most profound narcosis, and not until near death does it approach or fall below the normal, as the following records will show, which have been copied from kymographion tracings:

Exp. I. (*October* 5, 1880).—*Rabbit.*

Time. M. Sec.	Pulse in ten sec.	Remarks.
1.	37	
.05		Commenced inhalation by Woulfe bottle. The animal was previously curarized, and artificial respiration was resorted to, the apparatus being connected with the Woulfe bottle.
.15	37	
.55	38	
2.35	46	
3.15	48	
.55	45	
4.35	48	Anæsthetization complete. Maximum increase 11, or 29 per cent.

Exp. II. (*October* 6, 1880).—*Rabbit.*

Time. M. Sec.	Pulse in ten sec.	Remarks.
1.	45	Commenced inhalation as previously on an animal similarly rendered immovable.
.25	46	
.45	45	
2.05	47	
.25	48	
.45	58	
3.05	53	Animal anæsthetized.
.25	55	
.45	61	
4.05	54	
.25	47	
.45	54	
5.05	52	Maximum rise 16, or 35 per cent.

Exp. III. (*October* 7, 1880).—*Rabbit.*

Time. M. Sec.	Pulse in ten sec.	Remarks.
1.	33	
.05		Commenced inhalation with the use of the cone of muslin, it being held over the tracheal tube.
.20	37	
2.	38	
.40	45	
3.20	42	
4.		Added more ethylene to inhaler.
.40	48	
5.20	48	
6.	47	Respirations ceased.
.40	47	
7.20	45	
8.	47	Respirations commenced, but are shallow.
.40	44	
9.	46	Respirations became slower and deeper, and finally ceased. The heart continued beating for at least four minutes, and gradually ceased. Maximum increase 15, or 45 per cent.

Exp. IV. (*October* 9, 1880).—*Rabbit.*

Time. M. Sec.	Pulse in ten sec.	Remarks.
1.	36	
.03		Commenced inhalation by the use of the linen cone.
.07		
.32	39	
.42	39	Arterial pressure falling slightly.

Time. M. Sec.	Pulse in ten sec.	Remarks.
2.07	49	Arterial pressure rising slightly.
.27	46	The arterial pressure slowly rising; the pulse-curves are about one-third the height of the normal; the respirations are scarcely perceptible.
.47	46	Arterial pressure a little lowered, and equalling about seven-eighths of the normal.
3.07	48	
.27	46	Arterial pressure rising slightly.
.47	46	
4.07	48	Arterial pressure falling, and equalling about three-fourths of the normal.
.27	45	
.47	50	Arterial pressure falling slightly.
5.07	54	
.47	45	
6.07	46	
.27	48	Arterial pressure falling slightly.
.47	44	Arterial pressure falling, and equalling about five-sevenths of the normal.
7.		Added more ethylene to inhaler.
.07	46	
10.	45	
.20	46	
.40	46	
11.	46	
.20	45	
.55	46	
.58		Added more ethylene to inhaler.
12.15	46	
.35	46	
.55	46	
13.15	46	
.40	45	
15.	46	
17.	43	
20.	43	
.20	43	
.30		Added more ethylene to inhaler.
.40	45	
21.	50	
.20	48	
22.15	45	
.35	42	
.55	47	
23.15	45	
.35	43	Arterial pressure one-half of the normal.
24.15	43	
25.35	40	
26.05	42	
.25	47	
.45	42	
27.05	43	
27.25	42	Arterial pressure three-eighths of the normal. Maximum increase 18, or 50 per cent.

At the time of the conclusion of this record the pulse-curves had become so small as to be indistinguishable, and the tracing made by the marker was but a mere streak. When the fingers were placed on the chest of the animal, only a faint movement of the heart was perceptible, and the action of the viscus was more like tremors than distinct pulsations. The respirations at this time, if they were present at all, were so shallow as to be indiscernible.

The animal was allowed to remain undisturbed for about two minutes, and when a further examination was made the movements of the heart were found to be so feeble as to be almost inappreciable, and not the slightest respiratory movements were detected. The heart still possessing some vitality, it was thought that by attaching the artificial respiration-apparatus to the tracheal tube the respirations might possibly be restored and the moribund animal revivified. This was done, and after the lapse of two minutes not the least evidences of respiratory movements or of a restoration of the vitality of the almost paralyzed heart were present, and, as all signs of life save the almost imperceptible movements of the heart were gone, the animal was given up as being of no further use, and the artificial respiration-apparatus detached. In a few moments, however, it occurred to the writer that as this drug was probably both a cardiac and a respiratory depressant in toxic amounts, and that, as previously stated, death invariably occurred from a paralysis of the respiratory movements, we would have an invaluable antidote and revivifier in the nitrites if what the writer asserted in a recent article* was true, which was to the effect that the nitrites, in small or moderate doses, were powerful respiratory and cardiac stimulants. Although the long-continued absence of respiratory movements and the almost complete extinction of all the vital functions were points decidedly against a successful result of such an experiment, yet, while a negative result

* American Journal of the Medical Sciences, July, 1880, p. 158.

would not therefore materially disprove the above assertion, the opposite result would be strong, if not almost conclusive, testimony in its favor. The amyl nitrite was quickly obtained, and in a few moments several drops (probably five) were quickly injected into the tracheal tube, and the artificial respiration-apparatus again attached, so that the vapor of the nitrite would be forced into the lungs and thus become absorbed. In a few moments, to my intense gratification, the almost paralyzed heart seemed invested with a new life, and every moment its lost powers were being rapidly restored, the pulse-curves gradually increasing in height and volume, and in a less time than it takes to pen these notes were equal to the normal, and the heart was pulsating at the rate of forty beats in ten seconds, or four pulsations above the normal. The respirations did not recur for at least two minutes, and were then both shallow and slow, but in a few moments they had become so rapidly restored that they occurred at the rate of thirty-six per minute; two minutes later they were twenty-two per minute; at the seventh minute they were again thirty-six and the pulse in ten seconds forty-two; at the eleventh minute they were forty-two; at the fifteenth minute they were fifty-one and the pulse in ten seconds forty-two. Several drops of the nitrite were twice injected into the tracheal tube since the first recurrence of respiratory movements.

At the commencement of the inhalation of the amyl nitrite the arterial pressure was about one-third of the normal, and at the end of fifteen minutes it had not materially changed either one way or the other, although slightly lowered, which was quite contrary to what might be expected, since there was an augmentation of the frequency as well as of the force of the heart; but when it is remembered that the nitrites cause such intense vaso-motor dilatation, and that, notwithstanding the fact of their being decided cardiac stimulants, they cause a decided lowering of the blood-pressure in normal animals, the explanation of this apparent anomaly is evident. That we have in the nitrites an invaluable class of physiological antidotes for this compound is so clearly proven by the above as to need no further comment.

To return to the results of the preceding four experiments made on normal animals. It will be noticed that a decided increase in the pulse-rate invariably occurs, and that this increase continues far above the normal until immediately before death (Exp. III.), when it gradually failed, the increase being, respectively, 29, 35, 45, and 50 per cent., and the average about 40 per cent. The pulse-curves were diminished (Exp. IV.), and the arterial pressure decidedly lowered. In order to determine the *modus operandi* of this increased pulse-rate, it was first sought to decide whether the vagi apparatus was concerned: so the following experiment was made, in which both vagi nerves were severed, a tracheal tube was inserted, and the ethylene given by inhalation from a muslin cone, with the following result:

Exp. V. (*October* 13, 1880).—*Rabbit.*

Time. M. Sec.	Pulse in ten sec.	Remarks.
		Cut the pneumogastric nerves.
1.	35	
.03		Commenced inhalation.
.10	35	Arterial pressure reduced about one-tenth of the normal.
.30	34	
.50	34	
2.10	37	Pressure rose since 1.50, and is now about one-tenth of the normal above it. The respirations had now become very frequent, and for one minute the pulse-curves were not traced, only the respiratory curves.
		The respirations, which were normally seven in twenty seconds, are now increased to thirty-seven.
		The arterial pressure falls gradually until 3.15, when it reaches one-tenth below the normal; it then arose slightly, followed by a fall to the former point.
3.20	42	
.40	42	
4.	42	
.35	42	Pressure one-tenth below the normal, and gradually declining.
.55	42	
5.15	50	
.35	52	
.55	53	
6.30	46	
.50	45	
7.10	45	Pressure one-fourth below the normal.
.30	44	
.50	45	
8.25	46	
.45	45	

Time. M. Sec.	Pulse in ten sec.	Remarks.
9.05	46	Pressure about five-twelfths below the normal.
.25	46	
.45	47	
13.	45	
.20	46	
.30		Added more ethylene to inhaler.
.40	44	
14.	45	
.20	43	
.32		Respirations ceased.
.40	38	
15.	29	
.35	26	
16.15	27	
.55	28	
17.25	26	
.45	27	Since the fifteenth minute the pressure has gradually declined, and is now about one-fourth of the normal.
.55		The cardiac pulsations are so feeble as to be imperceptible, and at 18.25 the pressure fell to zero. Maximum rise 18, or 51 per cent.

It will be noticed that the result in this last experiment is identical with those made on normal animals, with the exception that a rise of the arterial pressure occurred which went above the normal. The pulse-rate was increased 51 per cent., which was as much as the greatest increase in any of the preceding observations, and, although the pulse-curves were not referred to in the preceding remarks, yet the same diminution of their size was apparent. It is therefore evident that the increased pulse-rate occurs independently of the pneumogastric nerves, and that it must be due either to a direct cardiac action or to a stimulation of the accelerator nerves. The determination of this point is satisfactorily accomplished by making, in the same animal, a combined section of both the cervical spinal cord and vagi nerves (in the section of the former the accelerator nerves are severed before their exit from the cord). This operation has been done in the two following experiments:

Exp. VI. (*October* 12, 1880).—*Rabbit.*

Time. M. Sec.	Pulse in ten sec.	Remarks.
1.	41	
.10		Commenced inhalation by Woulfe bottle.
.30	38	
.50	38	
2.40	35	
3.	34	
.20	36	
.40	40	
4.05	40	
5.	37	
7.	24	
9.	21	The pulse continues failing.

Exp. VII. (*October* 14, 1880).—*Rabbit.*

Time. M. Sec.	Pulse in ten sec.	Remarks.
1.	39	
.10		Commenced inhalation by Woulfe bottle.
.20	32	
.40	30	Pressure has fallen one-half of the normal, and is still declining.
2.15	35	
.35	27	
.55	20	
3.15	20	
.40	34	
4.	34	
.20	34	Pressure about one-third of the normal.

These results being directly the reverse of what has hitherto been recorded, it is very evident that the increased pulse-rate such as occurs in normal animals is dependent upon a stimulation of the accelerator nerves. Were it dependent upon the heart, the increase would still be apparent in animals operated on like the above, but which is not the result here; and it is an interesting fact to note that instead of the increase we have a diminution below the normal from the first; and the fact that the heart is isolated from the reception of any centric influences shows that the decline of the pulse is due to a depression of the heart itself. The consentaneous occurrence of a diminished pulse-rate, diminished pulse-curves, and diminution of arterial pressure decidedly indicates cardiac depression, and all three are undoubtedly due to this, unless it be that the diminution of arterial pressure may possibly, to a considerable extent, be due to vaso-motor dilatation.

A decided increase of the pulse-rate occurring in normal animals or in those having the accelerator nerves intact, and a diminution occurring in those in which the nervous connections of the heart were severed, is an exceedingly interesting point, and shows that the heart in normal animals is affected consentaneously in a dual manner, and that these two forces are in

constant antagonism, the one tending to cause an increase through a stimulation of the accelerator nerves, and the other a diminution by a direct paralyzant action on the heart. And it is evident that the effects of the stimulation of the accelerator nerves are more intense than those of the direct action on the heart: hence we have the increase. In two dogs, one in which the fibres of the accelerator nerves were cut a little below the medulla oblongata, and to which intravenous injections were given, the results, as the following records show, are confirmatory of what has already been stated.

Exp. VIII.—Dog.

Time. M. Sec.	Pulse in ten sec.	Remarks.
1.	16	
.10		Injected thirty minims intravenously.
.22		The blood-pressure fell rapidly to one-half of the normal; deep respirations and struggles sent it up to normal twelve seconds later; it then commenced to decline, reaching one-half of the normal at thirteen seconds later; and then commenced to rise gradually, reaching to within one-eighth of the normal at the fourth minute.
.40	23	
2.20	23	
.40	23	
3.	25	
.20	25	
.40	23	
4.20	22	
.40	23	
5.	22	
.20	21	
.40	19	
6.	20	
.20	19	
.40	20	Maximum increase 9, or 56 per cent.

Exp. IX.—Dog.

Time. M. Sec.	Pulse in ten sec.	Remarks.
1.	25	Cut the spinal cord a little below the medulla.
.05		Injected thirty minims intravenously.
.20	25	
2.	23	
.10	22	
.20	23	
.30	21	
4.	20	
.20	21	
.45	22	

The Effect on the Arterial Pressure.—When the ethylene is given by inhalation and by the modes already described, the arterial tension is but little affected during the first few minutes, unless the vapor be given in a very concentrated condition (Exp. X., XII., and XIII.), and then there is a very rapid decline, equalling nearly one-third of the normal, which is followed by a rise of half this amount, and then by a subsequent fall. In experiments where the air was heavily laden with the vapor (Exp. XIII.) essentially the same result occurred, but in the others, where the vapor was given more diluted, the fall of pressure is not nearly so marked, and the subsequent rise may nearly reach or even go above the normal. In Exp. XI., XII., and XIII. the animals were curarized to obviate any complications of the respirations, and the artificial respiratory apparatus, of course, employed. In Exp. X. the cone was kept almost saturated with the ethylene, and in Exp. XII. and XIII. sponges were placed in the bottom of the bottle, which were kept continually moistened with the liquid, and the air being driven through them, thus necessitating the absorption of considerable of the anæsthetic by the current of air.

Exp. X.—Rabbit.

Time. M. Sec.	Pressure. Mm.	Remarks.
1.	56	Commenced inhalation from a cone, which was kept wet throughout the experiment.
.07	52	
.32	39	
.42	32	
2.07	42	
.27	46	Respirations almost imperceptible.
.47	42	
3.07	40	
.27	46	
.47	45	
4.07	45	
.27	44	
.47	41	
5.07	41	
.47	45	
6.07	44	
.47	40	
7.07	42	Added more ethylene to inhaler.
10.20	42	
11.20	42	
.55		Added more ethylene to inhaler.

Time, M. Sec.	Pressure. Mm.	Remarks.
12.15	41	
.55	39	
13.40	38	
17.	37	
20.	36	
.30		Added more ethylene to inhaler.
21.	33	
23.	31	
24.	31	
25.	28	
26.	28	
27.25	27	No pulse-curves are distinguishable on the tracing.

Exp. XI.—Rabbit.

Time. M. Sec.	Pressure. Mm.	Remarks.
		Animal curarized.
1.	66	
		Commenced inhalation by means of the Woulfe bottle, in the bottom of which was placed about a drachm of ethylene.
.12	64	
.20	64	
2.20	63	
.40	63	
3.	61	
.20	61	
4.	61	
.40	56	Animal completely anæsthetized.
6.40	56	
7.	60	
.40	60	
8.	62	
.40		Dropped thirty minims ethylene in bottle.
9.	58	
.20	60	
11.20	56	
.30		Dropped thirty minims ethylene in bottle.
.40	57	
12.	58	
.10		Dropped thirty minims ethylene in bottle.
.40	53	
13.	48	
.10		Dropped thirty minims ethylene in bottle.
.20	47	
.40	51	
14.	45	

Exp. XII.—Rabbit.

Time. M. Sec.	Pressure. Mm.	Remarks.
1.	45	
.05		Commenced inhalation, using the Woulfe bottle as before.
1.25	44	
.45	46	
2.05	37	
.25	31	
.45	43	
3.05	45	Animal completely anæsthetized.
.25	46	
.45	47	
4.05	53	
.25	50	
.45	45	
5.05	41	
.25	40	
.45	37	
6.05	33	
.45	31	
7.45	31	
9.45	30	
10.05	29	Added ethylene.
.45	29	
11.25	28	Added ethylene.
12.05	26	
.25	23	
.45	22	
13.45	20	
14.25	18	
15.05	17	
.45	15	No pulse.

Exp. XIII.—Rabbit.

Time. M. Sec.	Pressure. Mm.	Remarks.
1.	54	
.10		Woulfe bottle used in which sponges were placed wet with the ethylene.
.20	54	
.45	52	
2.40	48	
3.20	44	
.40	48	Added more ethylene.
4.	48	
.40	49	
5.	47	
.20	44	
.40	50	
6.	52	
.20	48	
.40	48	
7.	44	
.20	31	
8.	25	
.40	32	
9.	32	
.20	25	
10.	19	
.40	17	
11.	15	

From these results it will be seen that the most pronounced effect of the ethylene on the blood-pressure when given by con-

tinuous inhalation, whether in a dilute or concentrated form, is to produce a diminution to zero, but which is transiently interrupted by a rise towards the normal, which is various in extent and may go even above it (Exp. XII.). As these changes in the pressure occur in curarized animals, any effect which altered respirations or muscular movements might have is obviated by this toxic condition; but as this diminution of pressure is accompanied by a frequent pulse and diminished pulse-curves, which latter has already been pointed out to be due to a depressed condition of the cardiac power, it is at once indicated that the fall of pressure is cardiac in its origin. However, several experiments made on animals with cut pneumogastrics gave results identical with those already recorded on normal animals. It therefore remained but to show whether the heart or vaso-motor system (or both) was the cause of the above results. Consequently, the heart being the most probable agency, experiments were made on animals in which the pneumogastric nerves and the cervical spinal cord were cut, which would necessarily sever all nervous connection with the heart, and whatever results would then follow would evidently be due to a direct cardiac action or to one on the peripheral vaso-motor mechanism.

Exp. XIV.—Rabbit.

Time. M. Sec.	Pressure. Mm.	Remarks.
1.	21	Cut the pneumogastrics and cervical spinal cord.
.05		Inhalation by Woulfe bottle.
.15	19	
.25	21	
.45	17	
2.05	18	
.25	17	
.45	15	
3.05	14	
.25	13	
.45	12	
4.45	12	
5.25	12	No pulse traced.

The fall of pressure still occurring, the following experiment was made to determine if the vaso-motor peripheries were concerned, and, in order to accomplish this object, the pneumogastric nerves and cervical spinal cord were severed and the thoracic aorta ligated, this latter operation cutting off communication of the blood with the major part of the vascular capillaries, and practically (for our purposes) annihilating the vaso-motor peripheries, while the section of the cord practically destroys the vaso-motor centres.

Exp. XV.

Time. M. Sec.	Pressure. Mm.	Remarks.
1.	53	Cut cord in upper cervical region; cut vagi and ligated thoracic aorta.
.05		Inhalation by Woulfe bottle.
.15	55	
.25	48	
.35	34	
.45	28	
2.05	23	
.25	25	
.45	24	
3.05	21	
.25	20	
.45	18	
4.25	16	
.45	15	
5.05	14	
6.25	13	
7.25	12	
8.25	11	
9.	10	
10.	8	No pulse traced.

The fall of pressure being still as marked in this last experiment, it must be concluded that the depression of the cardiac power is the cause of it, and, in further corroboration of this, it has been found that in animals whose thoracic cavity was opened the direct application of the ethylene to the heart caused its slowing or immediate arrest, and, further, that in animals slowly poisoned an autopsy revealed the heart arrested in diastole. It is probable, though, that the transient rise of pressure which interrupts the fall in normal animals is vaso-motor and both centric and peripheral in its origin, because it did not occur in either of the last two experiments; yet it was well marked in an experiment made on an animal with a cut cervical cord which has not been recorded in this paper.

In looking over the above series of experiments it is interesting to note that, although the drug is a direct and decided cardiac depressant, this organ is capable of bearing a considerable amount of depression before its complete paralysis, and, as was stated early in the paper, the respirations are always the first to succumb, and death is caused in this way. And it

was further found that if after the complete cessation of the respirations the artificial respiration-apparatus was attached and air laden with the ethylene vapor driven into the lungs the heart would still continue to pulsate for some minutes. After the blood-pressure had fallen almost to zero and the heart-beats could no longer be traced on the drum, yet when the thorax was opened the organ was still feebly pulsating, and continued so for several minutes. This fact is certainly an interesting one to remember, for in case of accident during its use, the absence of pulsations at the wrist would not be so serious as it otherwise would, and by reference to the text immediately following Exp. IV. the invaluable services to be looked for from the amyl nitrite cannot be overestimated. And in those cases where a sudden arrest of the respiratory movements occurs, the same good services can be expected, for it is evident, from the results of some of the preceding experiments, that the ethylene acts primarily as an excitant and secondarily as a depressant to the respiratory centres. That the respiratory movements must be arrested by centric paralysis is evident from the results of the experiment just quoted, for if it were due to a paralysis of the respiratory muscles, or of the nervous communication failing to convey the impulses from the centres, scarcely such a rapid recovery of full, regular, almost normal respirations could occur, since the nitrite acts as a depressant to both the motor portions of the cord and nerves and voluntary muscles. Yet the recovered respirations could be attributed to some extent, probably, to a greater supply of blood to the anæmic respiratory centres, for the reason that the increased force and frequency of the heart must have been the cause of driving considerably more blood through the centres, even if the blood-pressure was not increased and the respiratory centres were thus also indirectly stimulated by the nitrite. It is very evident that in the nitrites we have both respiratory and cardiac stimulants, and therefore a double physiological antidote by acting similarly upon the depressed heart and respiratory centres; and the importance of this knowledge cannot be too deeply impressed on the minds of those who will hereafter make use of this preparation.

As an anæsthetic for general surgical use it is undoubtedly superior to any yet introduced, with the exception of its isomeric compound ethylidene chloride and ether, and is inferior to the latter in but the single point regarding the relative degree of safety; and, while it in all probability is equal to chloroform in strength, promptness, and permanency of effects, it is fully as much superior to it in the point of safety as it is inferior to ether. This last is very evident by referring to the records of the experiments made on the arterial pressure, where it will be seen that the diminution of the arterial tension is that of a gradual decline, decidedly unlike that caused by the slow administration of chloroform, because of the absence of those wide and remarkable variations which occur, especially before complete anæsthetization. Also, when the vapor is given in a state of concentration by saturating a muslin cone with the liquid and placing it directly over the tracheal tube, as in Exp. X., although we have a decided fall of pressure, yet it does not immediately decline to zero, but consumes twenty-seven minutes in reaching within as many millimetres of it. Now let us turn to a similar experiment made with chloroform, and the difference in the results is strikingly great:

Exp. XVI.—Rabbit.

Time. M. Sec.	Pressure. Mm.	Remarks.
1.	59	Gave thirty minims of chloroform by inhalation from a muslin cone held over the tracheal tube.
.10	58	
.20	57	
.30	52	
.45	48	
.50	34	
2.00	18	
.10	12	No pulse.

The diverse and interesting results of these parallel experiments are so valuable as scarcely to be overestimated in a comparison of the relative safety of the two compounds, as the pulse in the ethylene experiment could be detected on the tracing for over twenty-five minutes, notwithstanding that the animal was continuously inhaling the vapor during the whole of this time, while in the chloroform experiment but a single dose was placed on the inhaler, the pulse-curves rapidly diminished in size, and the pressure fell to twelve

millimetres in a little over two minutes, and the pulse was extinct.

It needs no further argument to prove that this article (or, probably, ethydene chloride) should replace chloroform in such cases where ether cannot be used; but, as it is inflammable, care must be exercised in its use at night, and, as it is a cardiac and respiratory depressant (in toxic amounts), the same cautions should be observed in its use, and never should it be employed, if possible, without amyl nitrite at hand.

Before concluding, I take pleasure in expressing my indebtedness to Mr. Edward Hance (of the firm of Hance Brothers & White, Manufacturing Chemists, Philadelphia) for the presentation of this valuable ether for the purpose to which it was devoted. It is almost unnecessary to state that particular care was exercised in the manufacture of this specimen to have it pure.

Ethylene Ethylate and *Ethylene Methylethylate* were experimented with, and, although each of them possessed some slight anæsthetic powers, they were so feeble in this respect and caused such distress in breathing that they were abandoned as useless.

Ethyl Nitrate was used by Simpson,* who found it easy and pleasant to inhale, and to possess very rapid and powerful anæsthetic properties, and that small quantities, such as fifty or sixty drops, sprinkled on a handkerchief produced insensibility after a few inspirations. Shortly after, Nunnelly† stated that it possessed not much, if any, anæsthetic power; and my own experiments confirm this, as the following result will show:

"*Rabbit.*—Time, 12.32. Added one drachm to inhaler; .32½, struggles; .33, breathing deeper and slightly faster; .34, no change; .35, added a second drachm to inhaler; .35½, respirations again temporarily increased; .37½, orbital reflexes slightly diminished (?); .39, added a third drachm to inhaler; .40, respirations increased; .43, animal not anæsthetized, but somewhat drowsy, and, although the inhalation was continued for several minutes, no anæsthesia was produced."

Ethidene Dichloride, Ethylidene Dichloride, or *Ethylidene Bichloride* ($C_2H_4Cl_2$), which is isomeric with the ethylene bichloride, has of late attracted attention through the researches of the British Anæsthetic Committee,‡ who found that the exposed heart of the frog, in a glass jar containing an atmosphere impregnated with this vapor, continued beating slowly and regularly throughout the experiment, which lasted, in several cases, for twenty and twenty-six minutes respectively, although the animals were anæsthetized in from four to five minutes. In rabbits in which the thorax was opened and artificial respiration maintained, the cardiac contractions continued vigorous throughout the observations, which continued, in one instance, for forty minutes. Dogs were anæsthetized in from two to three minutes, and were kept fully anæsthetized for half an hour without the slightest failure of the respiration or heart. In experiments with the thorax opened and heart exposed (artificial respiration being kept up) no failure of the heart's action was observed, although the air passing into the lungs was saturated with the vapor. They further state that, practically, the animal can live for a prolonged period in a state of complete anæsthesia under the influence of the ethidene dichloride, while it dies in a short time under chloroform. And in six cases in which it was used§ they concluded that no injurious effects on the respiratory mechanism occur; that the pulse is lowered in frequency, but increased in volume, and in the deepest anæsthesia it was steady, regular, full, and compressible; that no failure of cardiac action was present, as they were led to anticipate in their experiments on animals; that there was never blueness of the lips or pallor of the countenance; and, lastly, that the anæsthetic "*presents all the advantages of ether without any of its disadvantages.*" In a more recent contribution‖ it is asserted that the *arterial pressure gradually but slowly fell,* and under repeated doses reached a minimum of twenty millimetres, and after prolonged and constant use was gradually brought down to seven millimetres.

Binz¶ used it in six experiments on man, and to his satisfaction, and found that when the patients were fully anæsthetized the breathing became spasmodic and shallow,

* Edinburgh Medical Journal, 1848, p. 741.
† Proceedings of the Provincial Medical and Surgical Association, 1849.

‡ British Medical Journal, 1879, vol. i. p. 1.
§ Loc. cit., p. 109. ‖ Loc. cit., p. 921.
¶ London Medical Times and Gazette, 1879, vol. i. p. 62.

the pulse lowered, but fuller and more compressible, and all of them presented the appearance of a strong cardiac stimulant. In two cases there was a rise in the pulse-rate, followed by a fall, and in a third case the pulse fell from ninety to eighty. The doses used varied from a drachm to a drachm and a half. More recently Reeve* has experimented with it, and his results "show a diminution of arterial pressure, not as occurs when chloroform is used, but, unlike it, it does not advance to complete extinction, nor are there such wide variations in effects at different times in the same animal as in the case of chloroform. . . . Snow believes that it will not be liable to cause sudden death, as chloroform sometimes does. In sixteen cases it did not cause nausea or vomiting, although food had recently been taken in several of them." Steffen† reiterates Snow's belief.

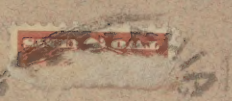
In making the above quotations the writer's object is threefold: first, to give sufficient detail, so that a just comparison can be made with the action of its sister compound, the ethylene bichloride, which the British committee stated to cause severe convulsions and no anæsthesia up to that time, while the ethidene dichloride promised to be "an excellent anæsthetic;" second, to call attention to the fact that it does cause a decided lowering of the arterial pressure, and, therefore, cannot "possess all the advantages of ether;" third, that a death has already resulted from its use.‡ It is probable that, while this anæsthetic is undoubtedly safer than chloroform and certainly more dangerous than ether, it bears a position of relative safety and power similar to that of its sister compound, the ethylene bichloride.§

* Chicago Medical and Surgical Examiner, June, 1880; quoted in New Remedies, 1880, p. 334.

† Binz's Evidences of Therapeutics, p. 39.

‡ Kappeler, Part XX., German Surgery, by Billroth and Luecke; quoted by Reeve, American Journal of the Medical Sciences, July, 1880, p. 216.

§ Another death from its use has been reported (British Medical Journal, May 29, 1880), and also several other cases in which alarming symptoms ensued.




POSTAGE